

## REMARKS

Withdrawn claims 13-30 have been canceled. Claims 3, 4 and 7 have been canceled. Support for the compounds presented in new claim 32 can be found, for example, in original claim 8 and in the specification. Applicants have amended previous claims to overcome various 35 USC §112 rejections as discussed below.

### Rejections under 35 USC §112, first paragraph

Claims 1-13 stand rejected under 35 USC § 112, first paragraph, because the specification allegedly does not reasonably enable "aryl" appearing in R1a, R1b, R2a, R2b, R3, R4, R5, R8, R9, R10, R11, R12, R13b, R14b, R15a and R15b.

It would only involve routine experimentation for one of ordinary skill in the art to make and use the invention. The burden is upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971) (holding that how an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance. The disclosure must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statement contained therein.) No such evidence or reason for doubting Applicants' disclosure is provided. Thus, the rejection is not supported.

The Office Action nevertheless alleges that the applicants do not synthesize compounds where "aryl" moieties can be found at positions other than R<sup>10</sup> or R<sup>11</sup>, for example. Although, no evidence or objective reasoning is provided as to why one skilled in the art would not be able to make such compounds. One of ordinary skill in the art would reasonably understand the meaning and metes and bounds of the "aryl" term, as used in the context of applicants' disclosure. Hypothetical stereo hindered compounds that cannot be made would be understood by one skilled in the art as not included within the scope of the invention.

"The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" See *Amgen v Hoechst Marion Roussel*, 65 USPQ2d 1385 (CA FC

2003). Making the compounds of the claimed invention having the "aryl" groups is routine for those of ordinary skill in the art. Thus, explicitly providing an example for preparing a species having an "aryl" group in a position other than R<sup>10</sup> or R<sup>11</sup> is not necessary to enable the same. See also, for example, Spectra-Physics v Coherent, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987) ("A patent need not teach, and preferably omits, what is well known in the art"); In re Howarth, 654 F.2d at 105, 210 USPQ 689 (CCPA 1981) ("An inventor need not ... explain every detail since he is speaking to those skilled in the art."); In re Gay, 309 F.2d 769, 774, 135 USPQ 311 (CCPA 1962) ("Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be.").

The specification, even though not necessary for an enabling disclosure, further provides numerous synthesis examples for preparing species of the claimed compounds. There is no requirement that an applicant provide examples directed to the preparation of each and every species of a claimed invention. See, for example, In re Angstadt, 537 F.2d at 502-03, 190 USPQ 214 (CCPA 1976) (deciding that applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art"); Utter v Higura, 845 F.2d at 998-99, 6 USPQ2d 1714 (CAFC 1988) (holding that a specification may, within the meaning of Section 112 Para. 1, enable a broadly claimed invention without describing all species that claim encompasses). Instead, as previously discussed, there is no requirement for any examples. See, for example, Marzocchi, supra, stating that "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology. is of no importance." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

Claims 2-12 and 31 are rejected under 35 USC 112, first paragraph as containing new matter. Claims 3, 4 and 7 have been canceled. In the interest of furthering prosecution, claims 2 and 5 have been amended to remove the structural variable for X and replace it with "CR<sup>10</sup>R<sup>11</sup> wherein one of R<sup>10</sup> and R<sup>11</sup> is H and the other is 2-methyl-4-thiazolyl". It is believed that this alleviates any possible confusion.

The Examiner objects to the use of the term "aryl" in R<sup>10</sup> and R<sup>11</sup> and alleges that the specification does not enable use of the invention commensurate in scope with the claims, that the claims are broader than the scope of enablement. Applicants disagree with this objection. As more fully discussed above, the instant specification contains a teaching of the manner and process of using the invention in terms that correspond in scope to the claims. However, in the interest of furthering prosecution the definition of R<sup>10</sup> R<sup>11</sup> has been amended to include the particular substituted or unsubstituted aryl radicals listed on page 8 of the specification.

Withdrawal of the rejections is respectfully requested.

Rejections under 35 USC § 112, second paragraph

The R<sup>10</sup> and R<sup>11</sup> variables in claims 1 and 9 have been amended to replace "aryl" with the substituted or unsubstituted aryl radicals found on page 8 of the specification and in the priority document. Claims 2 and 5 have been amended to define the variables for R<sup>10</sup> and R<sup>11</sup> when X=CR<sup>10</sup>R<sup>11</sup>. No new matter has been added. It is believed that the amendments to the claims render this rejection moot.

Rejections under 35 USC §103(a)

Claims 1-12 have been rejected under 35 USC 103(a) over CA 132:293587 and Nicolaou et al. Applicants respectfully traverse the rejection.

At page three, paragraph four, of the Office Action, the Examiner alleges that the claims contain new matter. With regards to the new matter rejection under 35 USC 103(a) it is not clear to the applicants exactly what new matter the Examiner is objecting to. The new matter rejection under 35 USC § 112 has been addressed above. No additional new matter has been defined. In any event, the existence of new matter does not warrant ignoring the claim recitations for purposes of claim analysis under §103.

The declaration provided by Dr. Klar clearly shows that it is advantageous to replace the 6(10)-methyl group present in naturally occurring epothilones with a higher alkyl. The data shows that representative compounds of the instant claim scope have advantageous antiproliferative properties and improved sensitivity to MDR cell lines compared to naturally occurring epothilone B and epothilone D. This showing is commensurate in scope with the current claims in view of the proviso in the claim 1 definition of  $R^{2a}$  and  $R^{2b}$ . The declaration evidence and applicants' previous remarks thereon should thus be fully considered. Nicolaou et al. provides no motivation to alter the structure to arrive at a genus wherein the  $R^{2a}$  or  $R^{2b}$  groups are ethyl or higher alkyl. Applicants have further amended the  $R^{2a}/R^{2b}$  proviso in claim 1. The proviso in the original claim reads "if -D-E stands for  $-CH_2-CH_2-$  or Y stands for an oxygen atom,  $R^{2a}/R^{2b}$  cannot be hydrogen/methyl". The use of the / is ambiguous and applicants have attempted to clarify this. Applicants submit that the recitation "whereby, if -D-E- stands for  $-CH_2-CH_2-$  and Y stands for an oxygen atom, at least one of  $R^{2a}$  and  $R^{2b}$  is not hydrogen or methyl" is fully supported by the instant disclosure. Although the exact words "whereby, if -D-E- stands for  $-CH_2-CH_2-$  and Y stands for an oxygen atom, at least one of  $R^{2a}$  and  $R^{2b}$  is not hydrogen or methyl" do not literally appear in the specification, such is not necessary for adequate written description; see In re Lukach, 169 USPQ 795 (CCPA 1971); Kennecott Corp. v. Kyocera International, Inc., 5 USPQ2d 1194, 1197 (Fed. Cir. 1987); Martin v. Johnson, 172 USPQ 391 (CCPA 1972); and In re Wertheim, 191 USPQ 90, at 98 (CCPA 1976). The original disclosure clearly encompasses compounds wherein "if -D-E- stands for  $-CH_2-CH_2-$  and Y stands for an oxygen atom, at least one of  $R^{2a}$  and  $R^{2b}$  is not hydrogen or methyl" see original claim 8 and the compounds shown in the original specification, for example. It would be clear there from, to one of ordinary skill in the art, that the original " $R^{2a}/R^{2b}$ " term was intended in the alternative, i.e., "at least one". Thus, the recitation "whereby, if -D-E- stands for  $-CH_2-CH_2-$  and Y stands for an oxygen atom, at least one of  $R^{2a}$  and  $R^{2b}$  is not hydrogen or methyl" does not bring the claims outside the originally disclosed scope. Similarly, the amendment made to the proviso in claim 1 herein is also supported by the original disclosure. The examples of specific species in the original disclosure make clear to one of ordinary skill in the art that the condition for -D-E- and Y giving rise to the proviso

should not have been in the alternative, but instead was a combined condition. For, example, the compounds (1(S or R),3S(E),7S,10R,11S,12S,14E/Z,16R)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione and (1R or S),3S(E),7S,10R,11S,12S,14E/Z,16S)-7,11-Dihydroxy-3-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-8,8,10,12,16-pentamethyl-4,17-dioxabicyclo[14.1.0]heptadec-14-ene-5,9-dione, recited in original claim 8 and the specification are not excluded by the corrected proviso but would have been under the original incorrect proviso.

It is urged that the currently recited proviso is fully supported by the disclosure. Claim 8 is amended to remove compounds excluded by the proviso into new claim 32.

Withdrawal of the rejection is respectfully requested.

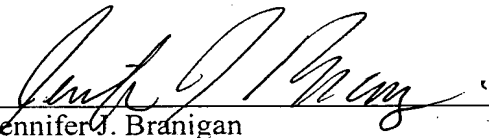
#### Double Patenting rejection

The Examiner has requested a Terminal Disclaimer over co-pending application 09/913,163 filed August 5, 2000. A terminal disclaimer was filed in the 09/913,163 application on March 9, 2005.

As for the alleged conflict with the claims of co-pending application 10/631,011, the '011 claims are drawn to a specific Effector Conjugate. The '011 claims require at least one substituent L1, L2 or L4 which represents a linker of general formula III or IV. The compounds of the present claims do not include any such linker. Thus, the current claims are not obvious variants of the claims of the '011 application in any way.

In view of the above remarks, it is respectfully submitted that the claims of the application are fully supported by the specification and as such are in order for allowance.

Respectfully submitted,

  
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